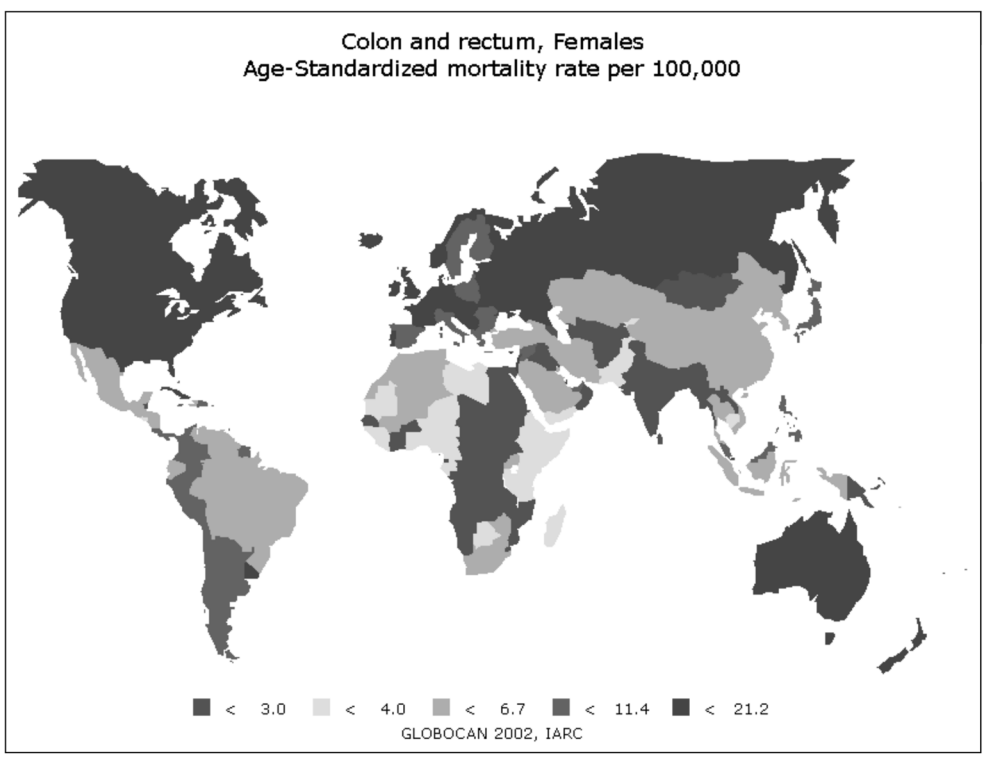
2. DESCRIPTIVE EPIDEMIOLOGY OF COLORECTAL CANCER. VARIATIONS AND TRENDS

Aleksander Galas

Cancer was estimated to account for about 7 million deaths worldwide and about 10 million new cases in 2000 (1). It is the third most common cause of death in the world after cardiovascular and infectious diseases. Cancer is also estimated to be responsible for 6% of the global burden of diseases (2). Approximately, 70% of all cancer deaths occurred in the developing countries (3), however, ageing of the population, and good control of communicable diseases substantially increased cancer-related proportional mortality in the developed countries. Moreover, there is expected further increase in cancer mortality by about 70% in the developing and about 30% in the developed countries (4).

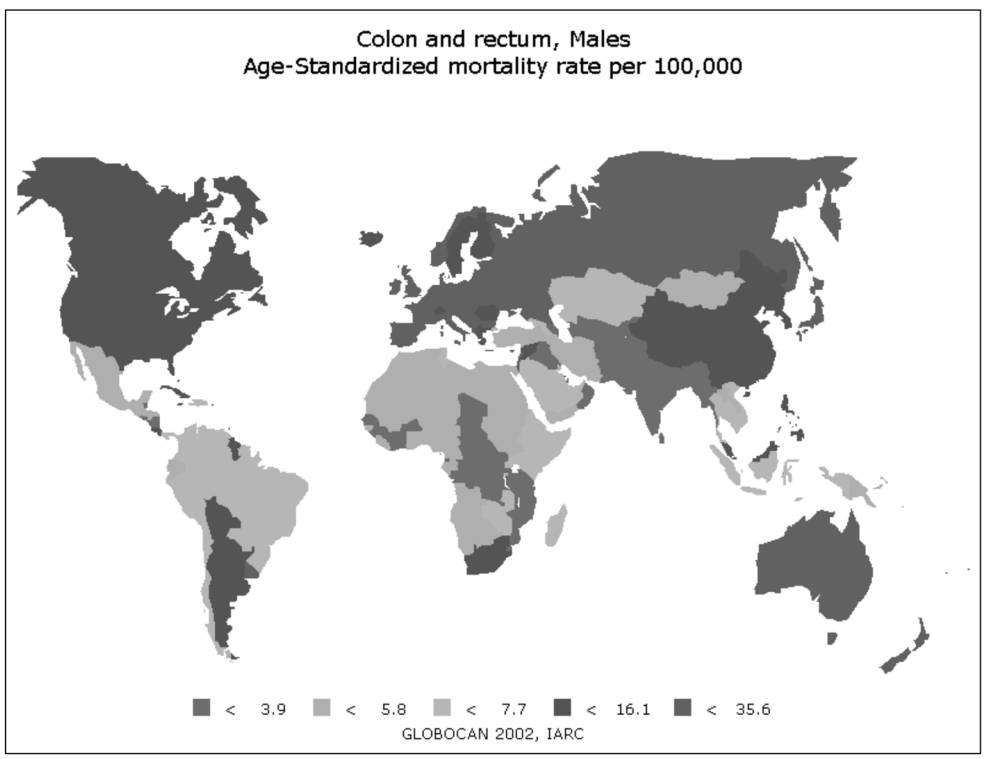


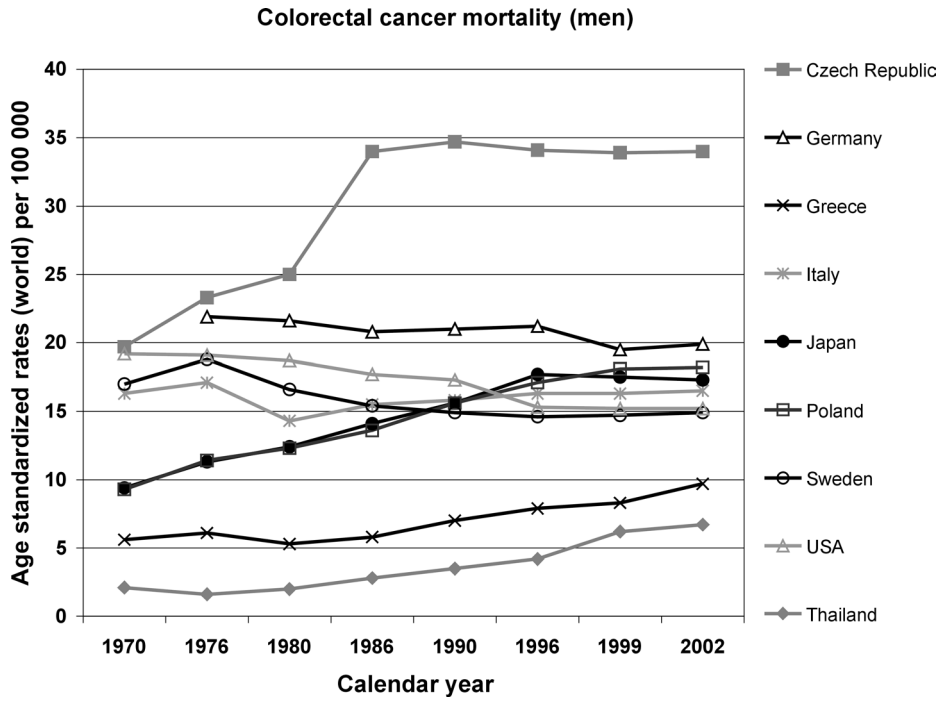
Colorectal cancer in one of the most common cancers worldwide responsible for approximately 579 000 deaths/year (8.4% of all cancers deaths), preceded only by 1 213 000 trachea, bronchus and lung cancer-related deaths (17.5%), 744 000 due to stomach cancer (10.7%), and 626 000 due to liver cancer (9.0%) (5). The numbers of colorectal cancer deaths vary across the world and are closely related to the level of development in the region. Colorectal cancer mortality and morbidity rates are about 5 to 10-fold higher in the developed than in the developing countries.

In Poland, colorectal cancer accounts for approximately 4500 deaths among men and 4200 among women. Age-standardized mortality ratio increased in Poland from 6,1/100 000/year in 1963 to 18,0 in 2000 among men and from 5,0 to 11,0 in women in the same time (6, 7).

Similar rising tendency has been observed in other countries as well (8, 9). Thus, one of the highest mortality rates due to colorectal cancer has been observed in the Czech Republic as a result of rapid increase between 1970–1990 after which the rates stabilized at the relatively high level. Otherwise, in some countries in the West and North Europe very slow, but consistent decrease in mortality pattern has been observed.

Colorectal cancer mortality trends in Poland are similar to those in Japan, where mortality rates for men increased from below 10/100 000/year in 1970 to about 17.5 in 1996 and thereafter stabilized. In Poland, however, slight increase in colorectal cancer mortality in men after 1996 has been noted. The lowest mortality rates are reported from Africa, Central America, Central South and Eastern Asia and relatively low from Greece. However, in all these regions steady rise of rates has been reported.



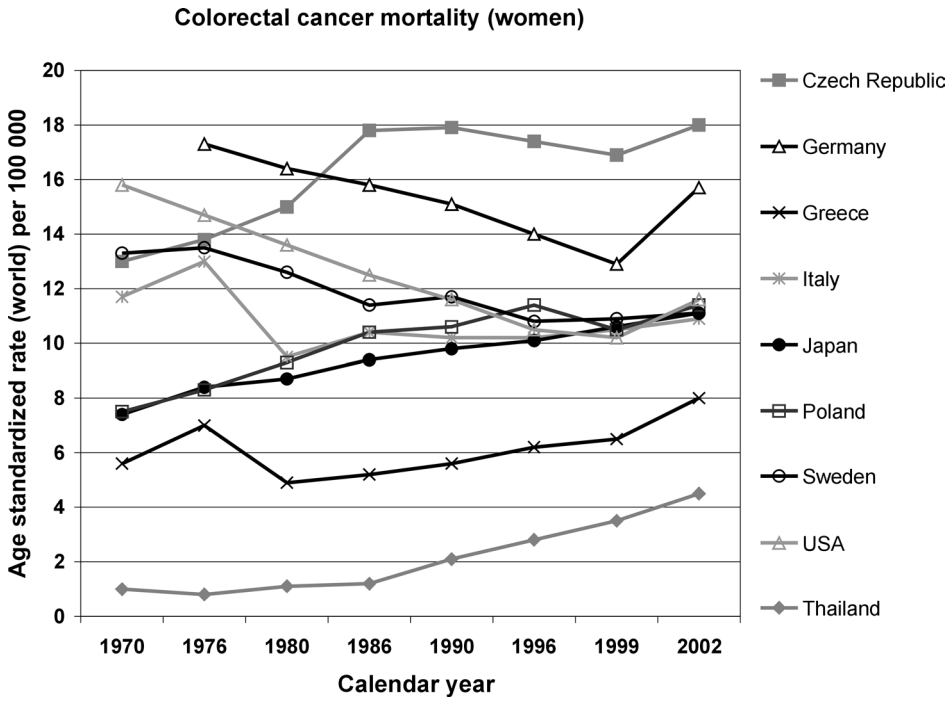


Regional variability of colorectal cancer-related mortality in women and men is similar. Mortality rates in men are about 50% higher than in women with steadily increasing tendency observed worldwide. In Poland, colorectal cancer age-standardized mortality almost doubled within the past 35 years. In the Czech Republic, after rapid increase of colorectal-cancer related mortality between 1970–1990, and a small decline in 1990–1999, the rates stabilized and were comparable with those highest in the world. Steady increase has been reported also from the countries with relatively low mortality rates observed earlier (e.g., Greece, Thailand). Moreover, declining colorectal cancer mortality patterns until 2000 observed in the USA and Western Europe reflected growing tendency thereafter.

The global burden of cancer in general and also for colorectal cancer may be more serious than mentioned above, since according to Mathers the rates of the cancer mortality are underestimated (10).

Although mortality rates seem to provide precise information because the causes of deaths are accurately collected and mortality databases are easily available, the incidence provides more valuable estimates, since it does not depend on the ability of the health care system to effectively cure the disease.

The Global Burden of Disease 2000 project showed, that colorectal cancer is the third most common cancer across the world and accounts for 8.9% of cancer cases (11). There are more than 917 000 new colorectal cancers annually worldwide, with about 377 000 new cases in Europe, 242 000 in Western Pacific and 160 000 in America. It was confirmed that colorectal cancer incidence increases with the level of the development in the region.

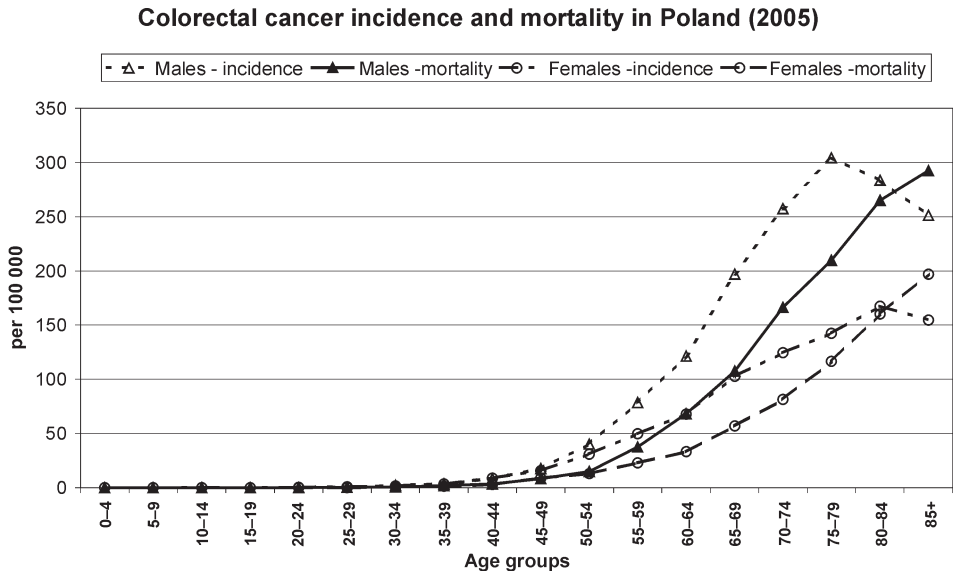


In Poland in the past 40 years 3-fold increase in colorectal cancer age-standardized incidence among women (from 5.5 in 1963 to 15.9/100 000/year in 2005) and 4-fold among men (from 6.2 in 1963 to 27.4/100 000/year in 2005) was observed.

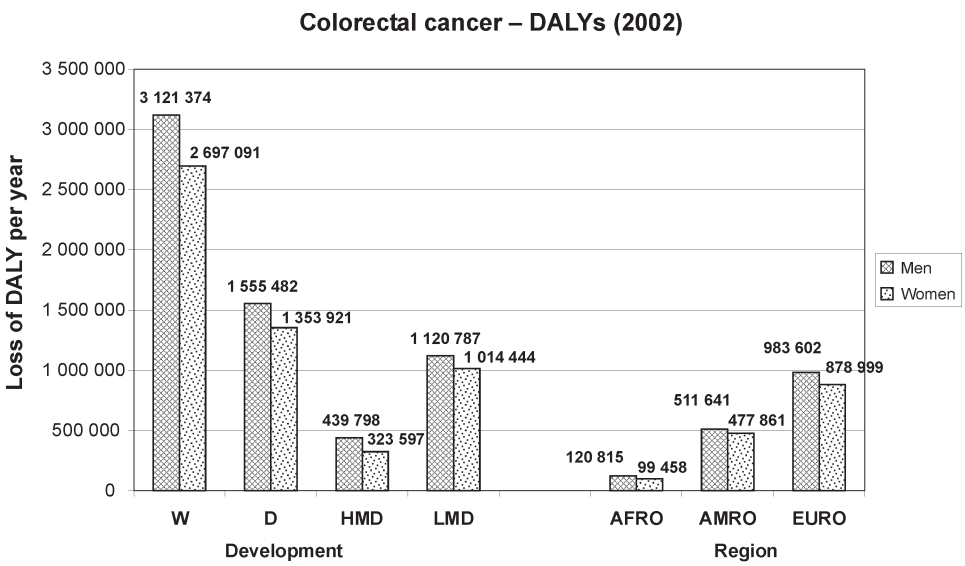
Cancer of colon and rectum is age-specific. Colorectal cancer incidence rates in Poland rapidly increase among people after the age of 50 and stabilize at the age of 80, exceeding 250/100 000/year for men and 150/100 000/year for women. Mortality rates are reflecting growing tendency throughout the life span, reaching 292.7 colorectal cancer deaths/100 000/year among men at the age 85 and over, and 197.1 deaths/100 000/year among women in the same age group.

Measures (like cancer mortality and incidence) presented above, despite being widely used, have some disadvantages. They do not take into account consequences of the disease other than death, like impairment, disability or handicap. Therefore, other measures, like DALY, were created. DALYs for a disease are the sum of the years of life lost due to premature mortality (YLL) in the population and the years lost due to disability (YLD) for incident cases of the health condition. Thus, the DALY is a health gap measure that extends the concept of potential years of life lost due to premature death (PYLL) to include equivalent years of 'healthy' life lost in conditions broadly termed disability. One DALY represents the loss of one year of equivalent full health.

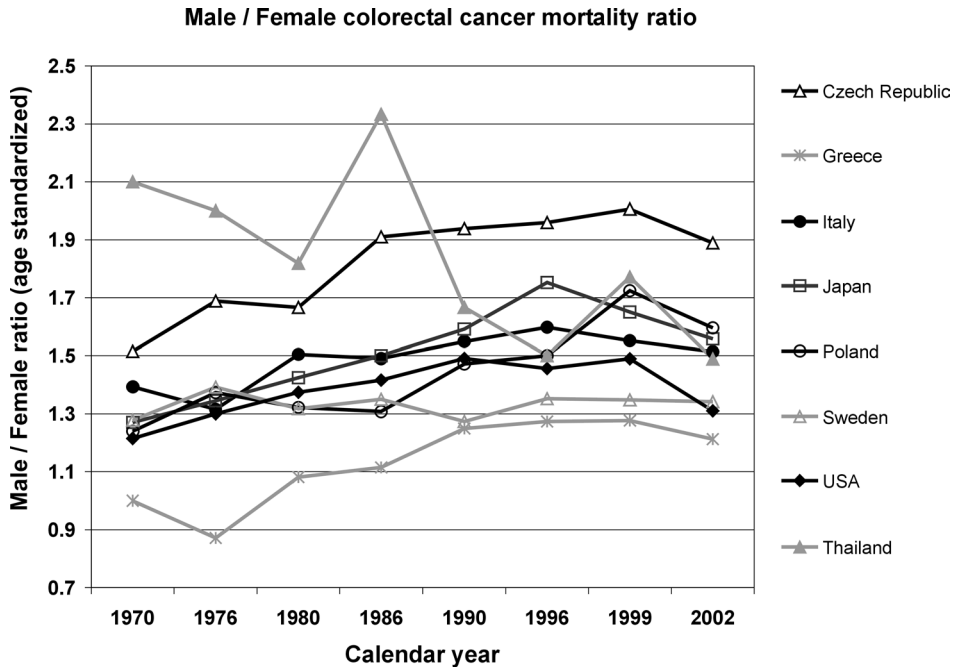
The global loss of DALY related to colorectal cancer is estimated as 3 121 000 in men and 2 697 000 in women. Since colorectal cancer is typically observed in the developed communities, thus the majority of losses of DALYs is observed in the developed (males – 1 555 000; females – 1 354 000) and in the low mortality developing countries (males



– 1 120 000; females – 1 014 000). The estimated loss of DALYs in the European region is 983 000 for men and 879 000 for women. In Africa 121 000 loss of DALYs for men and 99 000 for women were registered. Most of the losses of DALYs are attributable to premature deaths. The estimated YLDs are only 309 000 for men and 301 000 for women, accounting for about 10% of DALYs. In the high mortality developing countries YLDs are only 8000 for men and 9600 for women.



W – world; D – developed; HMD – high mortality developing; LMD – low mortality developing; AFRO – African region, AMRO – American region; EURO – European region



Although the frequency of colorectal cancer seems to be similar among men and women, the male/female pattern of colorectal cancer mortality changes over time. Before 2000 increasing trends in male/female (M/F) ratio were observed across the world, however, the degree of change varied across countries. During the past thirty years in Sweden the M/F ratio increased only by 6%, in Italy by 11%, but in Greece, Japan and Czech Republic the change was even larger, and reached 30%. In Poland increase in M/F colorectal cancer mortality ratio was even higher reaching 39% (from 1,24 to 1,72), however, after 2000 the decrease was observed.

Probably smaller progression in age-adjusted colorectal cancer mortality among women is responsible for the change in the M/F colorectal cancer mortality ratio. However, this relationship was observed till 2000, but thereafter age-adjusted colorectal cancer mortality clearly rose among women, and stabilized in men allowing M/F mortality ratio to decrease. It is not clear what other factors may be responsible for the changes.

There are a lot of prevention programs implemented across the world, but increasing colorectal cancer mortality is still observed. Up to date it is difficult to estimate whether observed trends could be artefactual or whether they reflect growing risk of colorectal cancer across populations. The procedures related to establishing diagnosis and registering cancer cases have improved over time, and being more sensitive may partially influence observed changes of the rates. On the other hand, growing numbers of the identified colorectal cancer risk factors may be even more plausible. Genetic susceptibility and differences between sexes account for the differences in M/F colorectal cancer mortality ratio. These ambiguities point to the need for the detailed studies in the future.

Although increasing trends in colorectal cancer incidence and mortality are mostly associated with the known risk factors and their interactions with genetic susceptibility, the selection of diagnostic tools used over the past decades may also have effect. Some of the methods were unavailable fifty or thirty years ago. For example, the use of diagnostic colonoscopy substantially increased the number of performed polypectomies to remove colorectal polyps, which might in fact be precancerous lesions. In this way, the number of diagnostic colonoscopies performed in a given population may lower the incidence rate of colorectal cancer analyzed in future for this particular group. Wide use of screening tests shifts the time of diagnosis of colorectal cancer to early stages which is reflected in the higher incidence rates over this particular time period.

Colorectal cancer may have different origin and different localization in the colon, i.e., in caecum, ascendent, transverse, and descendent colon, hepatic or splenic flexures, sigmoid colon and rectum. Over the past 30 years tumours of the right colon have been considered more common (12, 13, 14). The interpretation of these findings may be difficult due to many reasons. First of all, the study samples contained relatively large proportion of site unspecified tumours. There is evidence showing that tumours of the right colon are over represented among women in the West Europe countries (15). The investigators used different classifications of the left and right sided-tumours, and finally, frequency distributions presented for the sub-locations were not age-standardized and not all series were population based.

There are large geographical differences in the mortality and morbidity observed across the World. The incidence of colorectal cancer varies by 25-fold between the regions with the highest and the lowest frequency. The loss of DALYs also shows large variations. Most of the authors attributed these discrepancies to diet-related factors, as responsible for up to 80% of colorectal cancer cases. However, genetic predisposition, environment and other life-style factors may also play important role in the colorectal cancer pathogenesis and development. Up to date there are different opinions concerning etiology, pathogenesis, and genetic predisposition in the colorectal cancer, thus systematic, collaborative, international investigations are needed to unravel this (16).

References

1. Revised Global Burden of Disease (GBD) 2002 Estimates. Health statistics and health information systems. WHO. http://www.who.int/healthinfo/bodgbd2002revised/en/index.html.
2. Global Burden of Disease Estimates. Health statistics and health information systems. http://www.who.int/healthinfo/bodestimates/en/index.html.
3. Parkin DM, Whelan SL, Ferlay and Storm H. Cancer Incidence in Five Continents, Vol. I to VIII. IARC Cancer Base No 7, Lyon 2005.
4. Pisani P, Parkin DM, Bray F, Ferlay J. Estimates of the worldwide mortality from 25 cancers in 1990. *International Journal of Cancer* 1999; 83(1): 18–29.
5. Health statistics and health information systems. http://www.who.int/healthinfo/boddaly/en/.
6. Zatoński W, Tyczyński J (ed.). Cancer in Poland in 1995. Pracownia Poligraficzna Centrum Onkologii – Instytutu im. Marii Skłodowskiej-Curie, Warszawa 1998.
7. Didkowska J, Wojciechowska U, Tarkowski W, Zatoński W. Cancer in Poland in 2005. Promocja XXI, Warszawa 2007.
8. Globocan 2000.

9. Bosetti C, Malvezzi M, Chatenoud L, Negri E, Levi F, La Vecchia C. Trends in Colorectal Cancer Mortality in Japan, 1970–2000. Letter to the Editor. *Int J Cancer* 2005; 113: 339––341.
10. Mathers C, Boschi-Pinto C. Global burden of cancer in the year 2000: version 1 estimates. www.who.int.
11. Murray CJL, Lopez AD, Mathers CD, Stein C. The Global Burden of Disease 2000 project: aims methods and data sources. GPE Discussion Paper No 36. WHO, Geneva 2001.
12. Devesa SS, Chow WH. Variation in colorectal cancer incidence in the United States by subsite of origin. *Cancer* 1993; 71: 3819–3826.
13. Jass JR. Subsite distribution and incidence of colorectal cancer in New Zealand, 1974–1983. *Dis Colon Rectum* 1991; 34: 56–59.
14. dos Santos Silva I, Swerdlow AJ. Sex differences in time trends of colorectal cancer in England and Wales: the possible effect of female hormonal factors. *Br J Cancer* 1996; 73: 692–697.
15. Thorn M, Bergstrom R, Kresser U, et al. Trends in colorectal cancer incidence in Sweden 1959–93 by gender, localisation, time period, and birth cohort. *Cancer Causes Control* 1998; 9: 145–152.
16. World Cancer Research Fund/American Institute of Cancer Research. Food, nutrition and the prevention of cancer: a global perspective. Washington: WCRF/AICR.